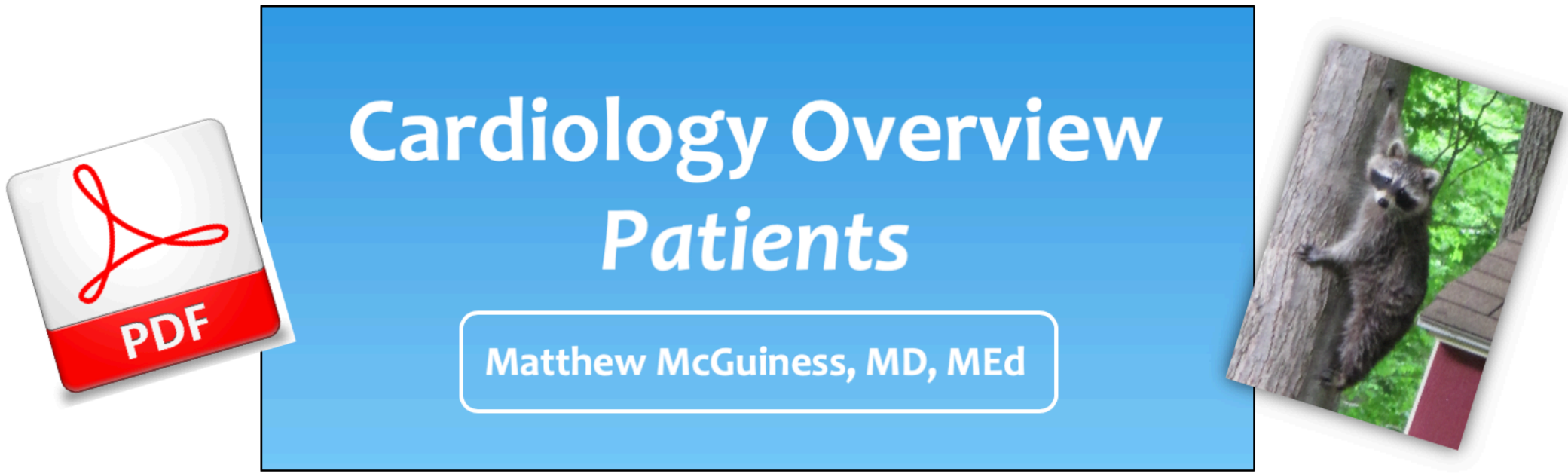
Cardiac Electrophysiology for the USMLE Step One Exam



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Cardiology Overview
Patients

Matthew McGuiness, MD, MEd

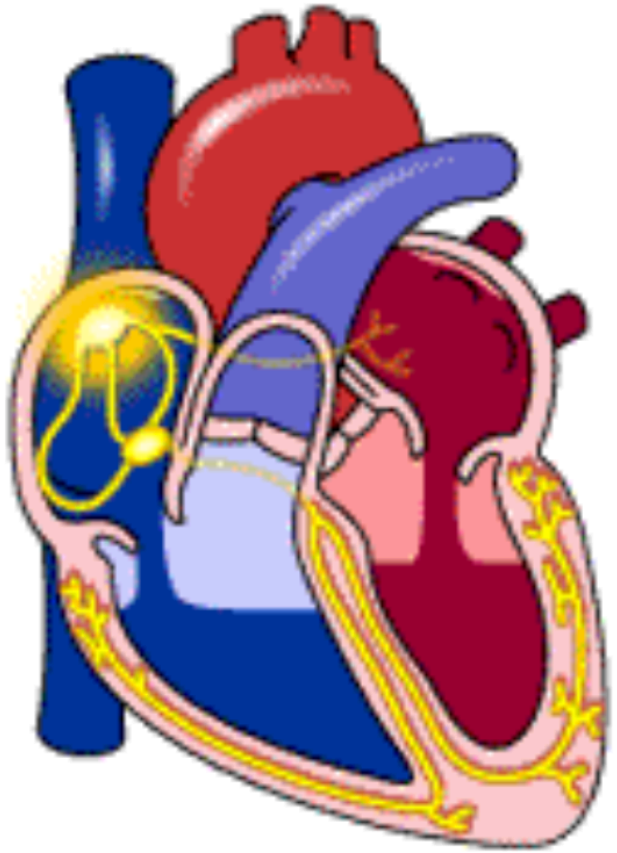
Outline

* Cardiac electro-mechanical function
  * Electrophysiology and myocyte function
  * Pump function and hemodynamics

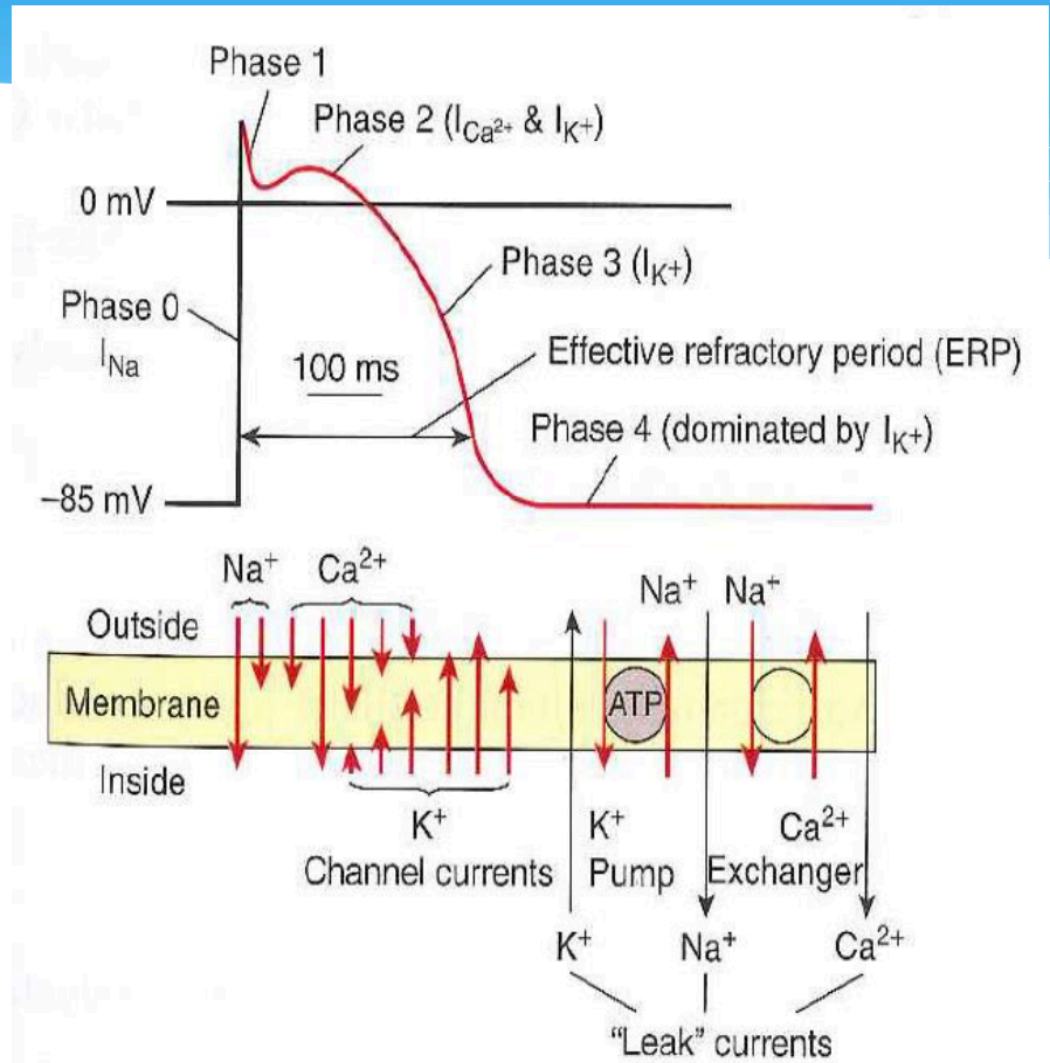
* Cardiac rhythm disturbances and antiarrhythmic drugs

Two Major Elements of Pump Function

* Electrical system
  * Generates spontaneous activation
  * Rapidly disperses activation wavefront
* Mechanical system (myocytes)

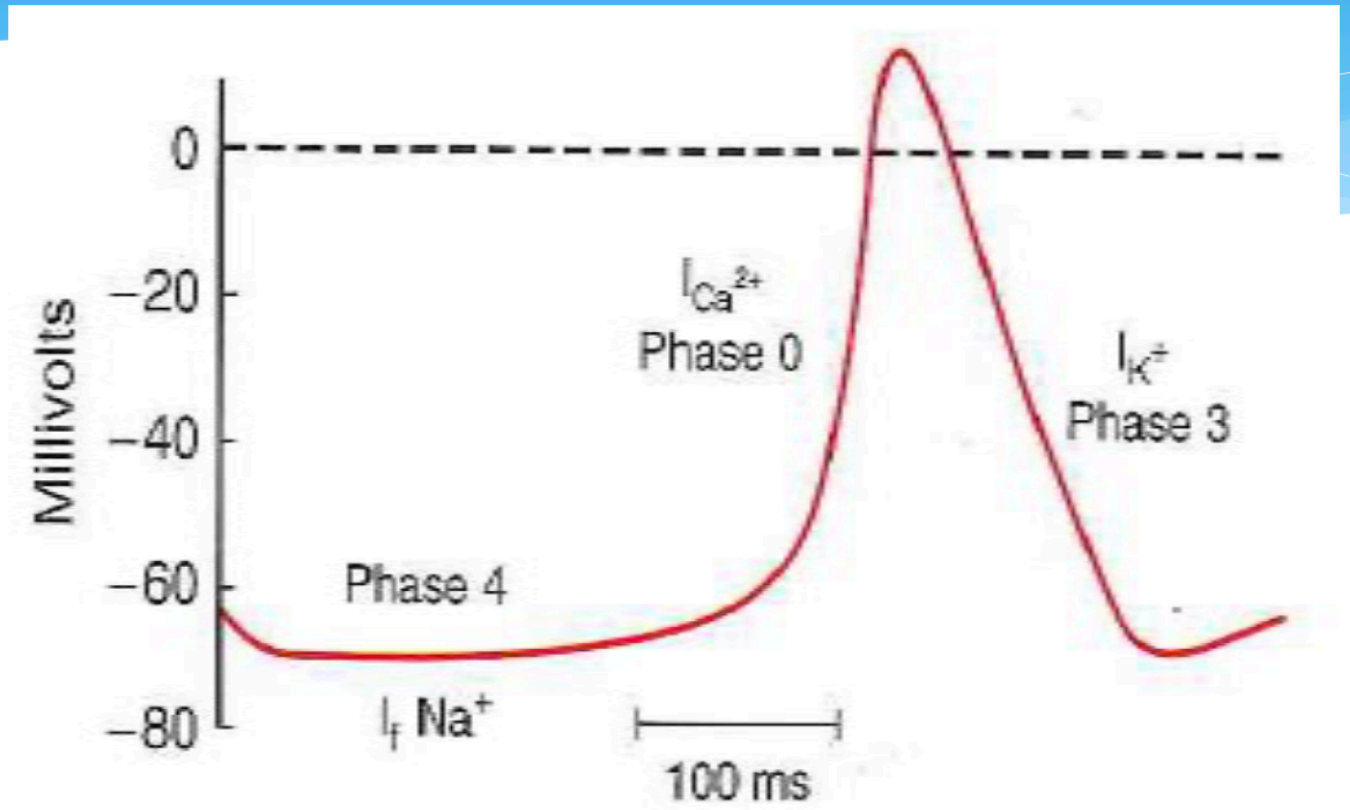


Cardiac Action Potential



Le, et. al. First Aid for the Basic Sciences: Organ Systems. 2012

Cardiac Action Potential



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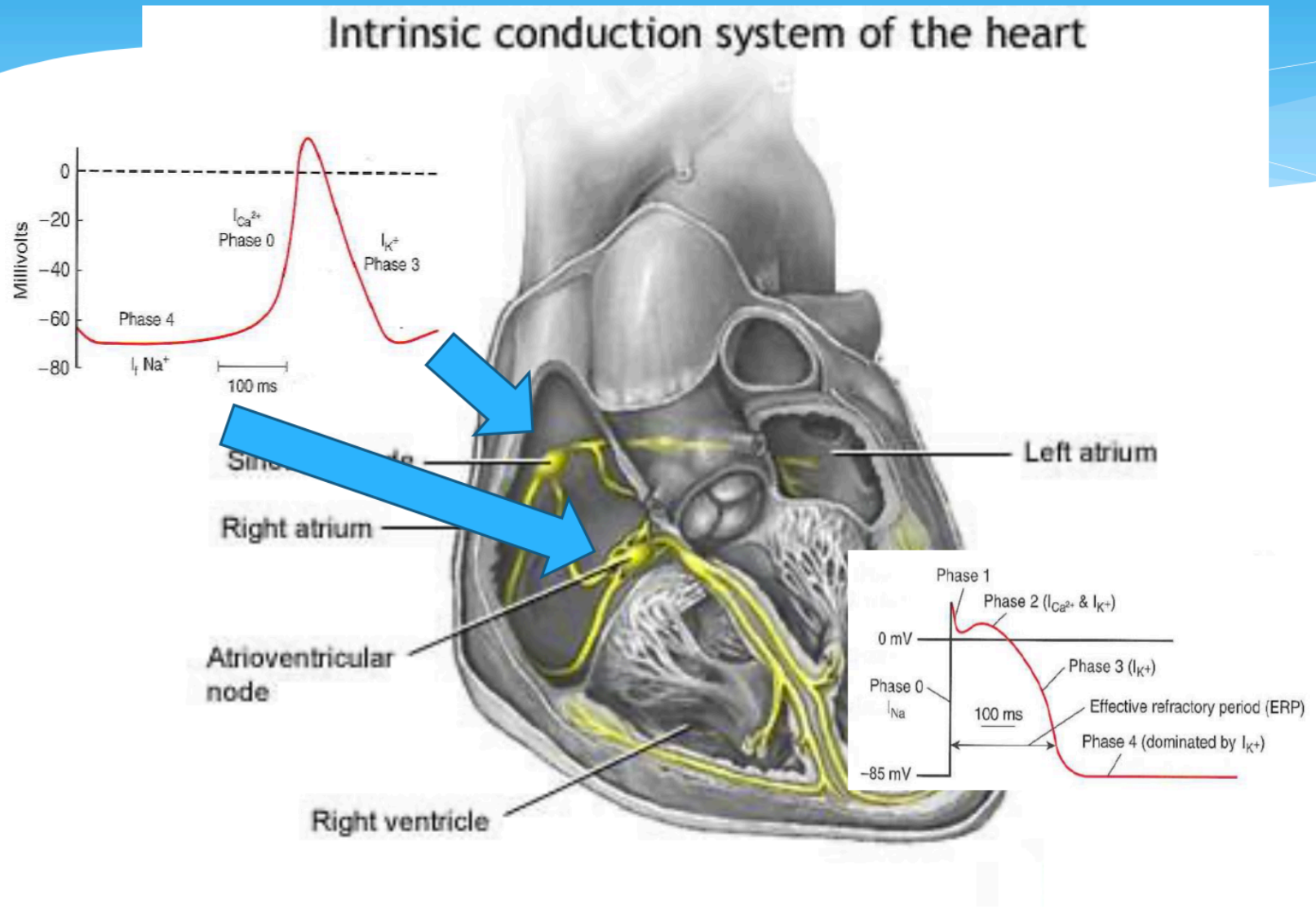
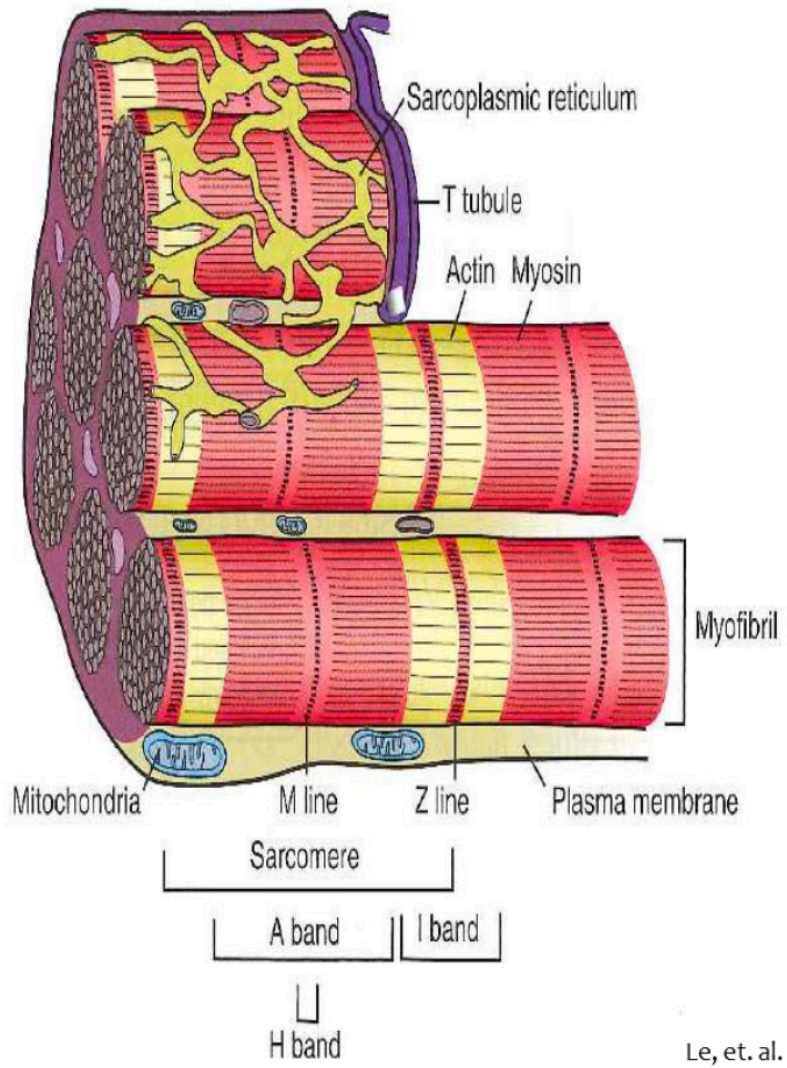
Putting it together…



Myocyte Structure



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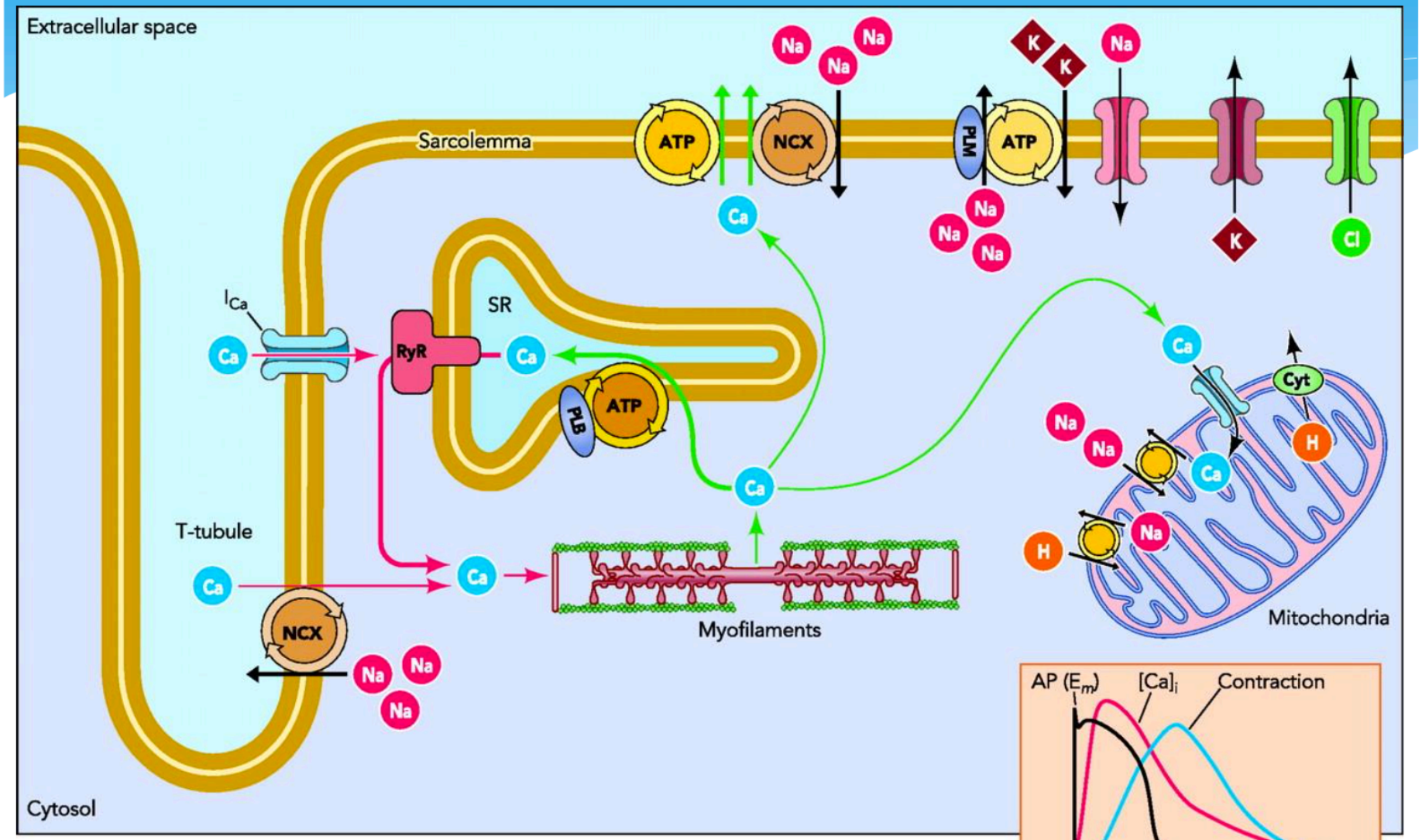
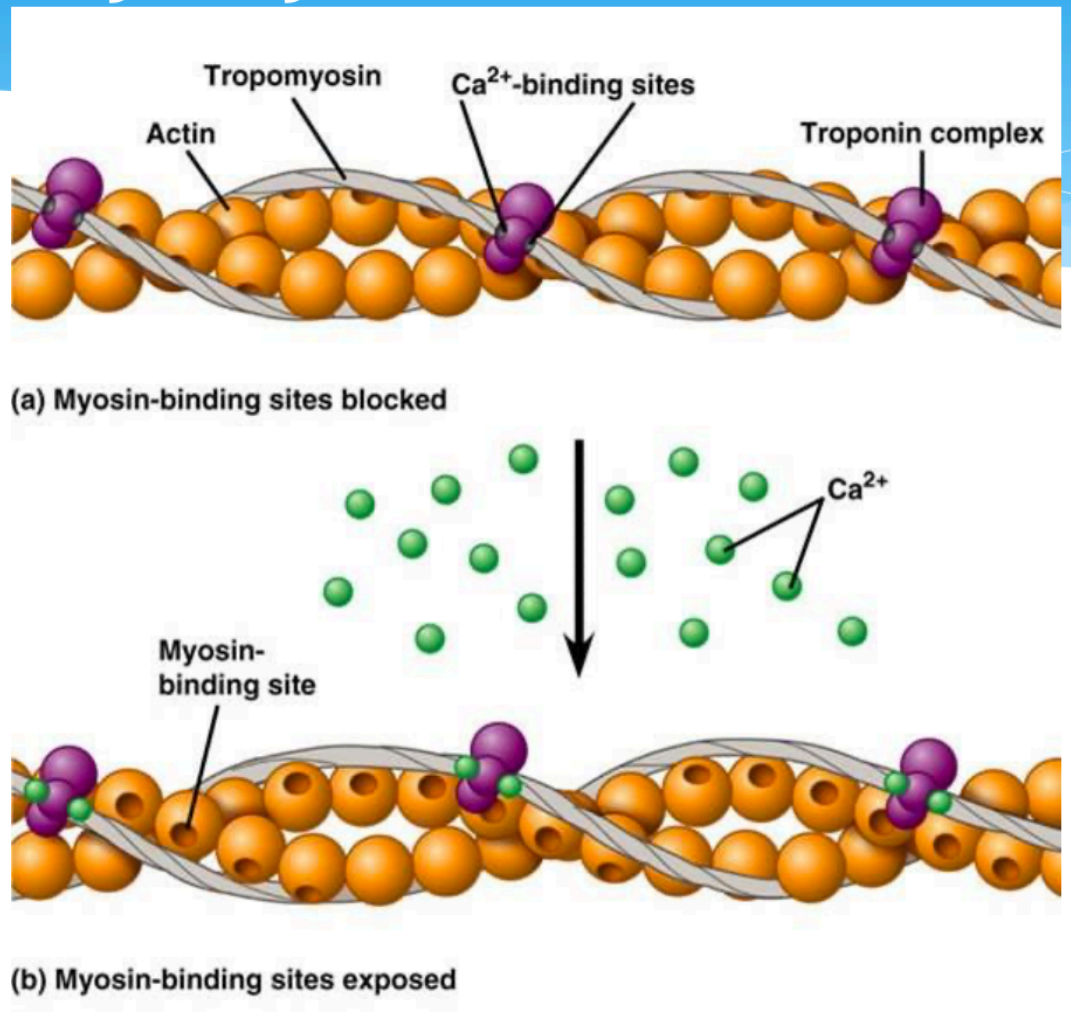
Myocyte Contraction



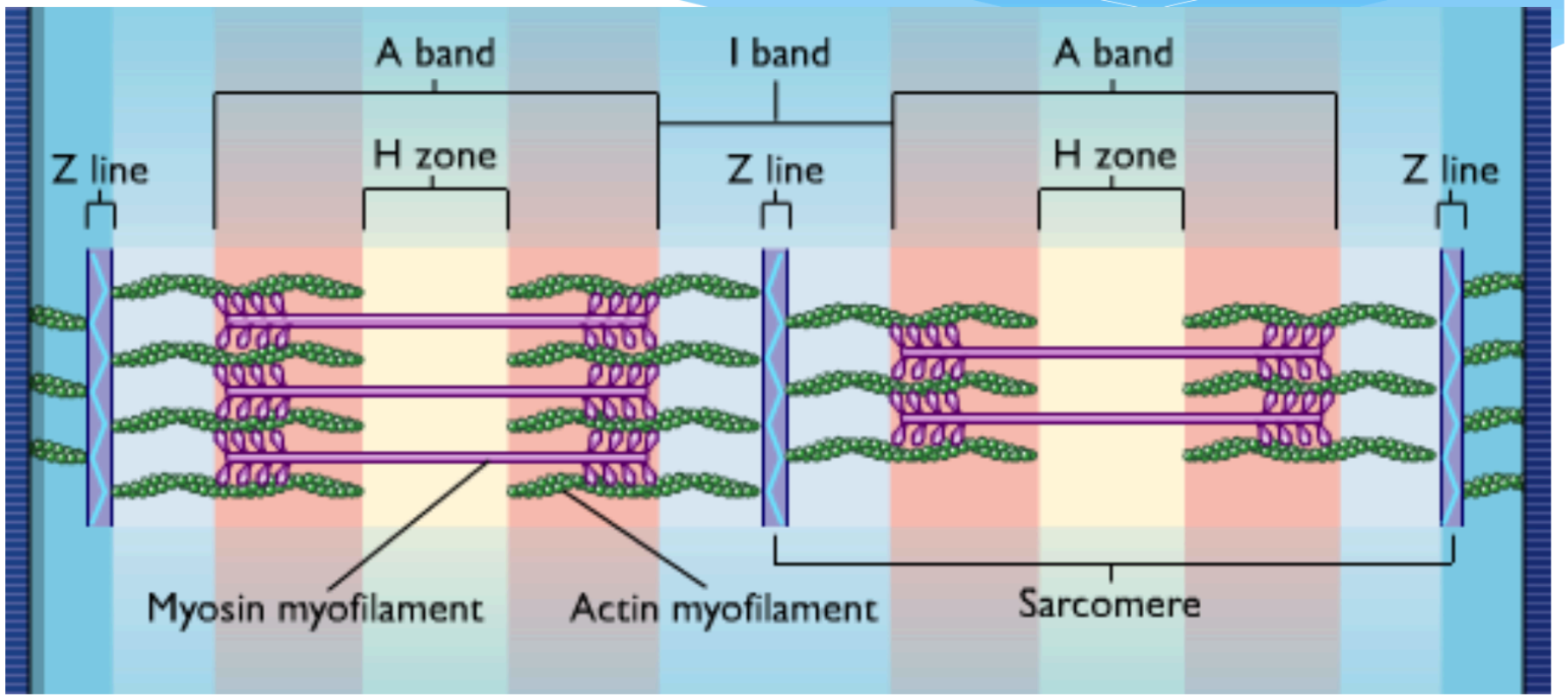
http://physiologyonline.physiology.org/content/21/6/380/F1.expansion.html

Myocyte Contraction



http://www.aandptutor.com/semester-1-ap/muscles-2/sliding-filament-model/

Myocyte Contraction



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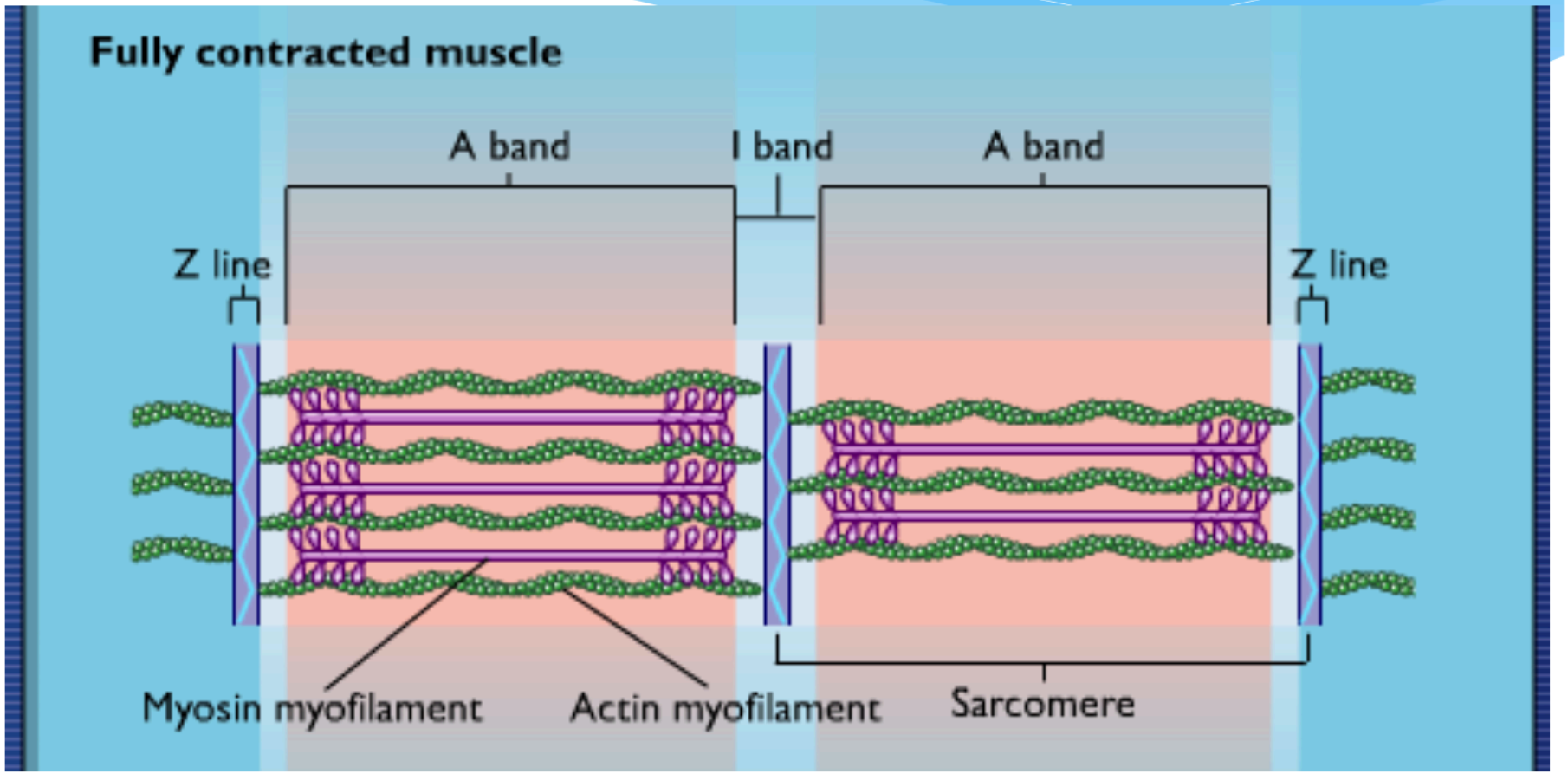
Myocyte Contraction



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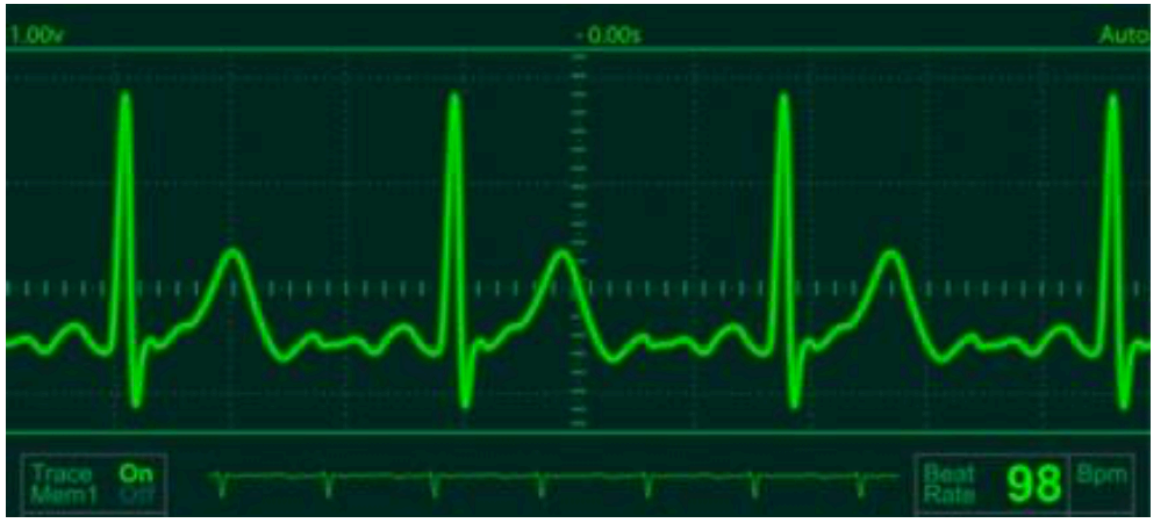
Cardiac Rhythm Disturbances and Antiarrhythmic Drugs

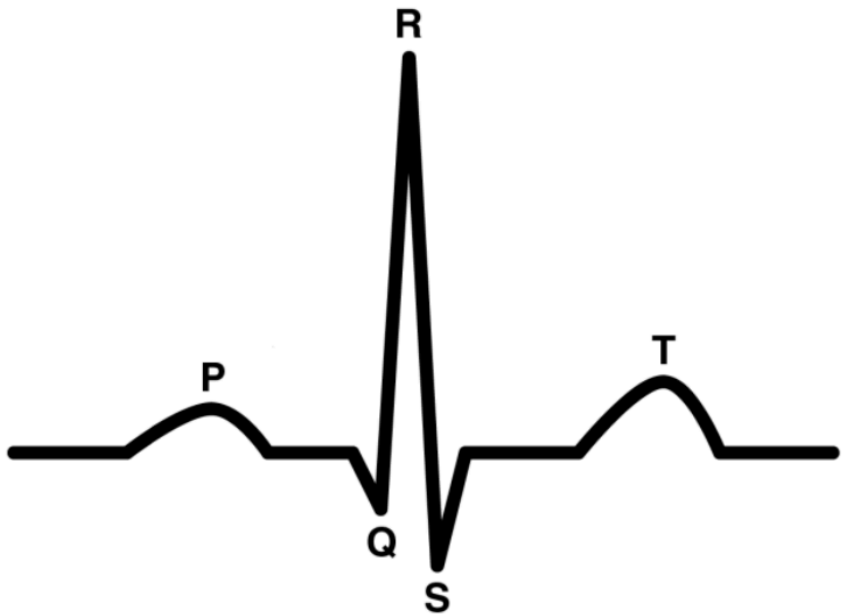


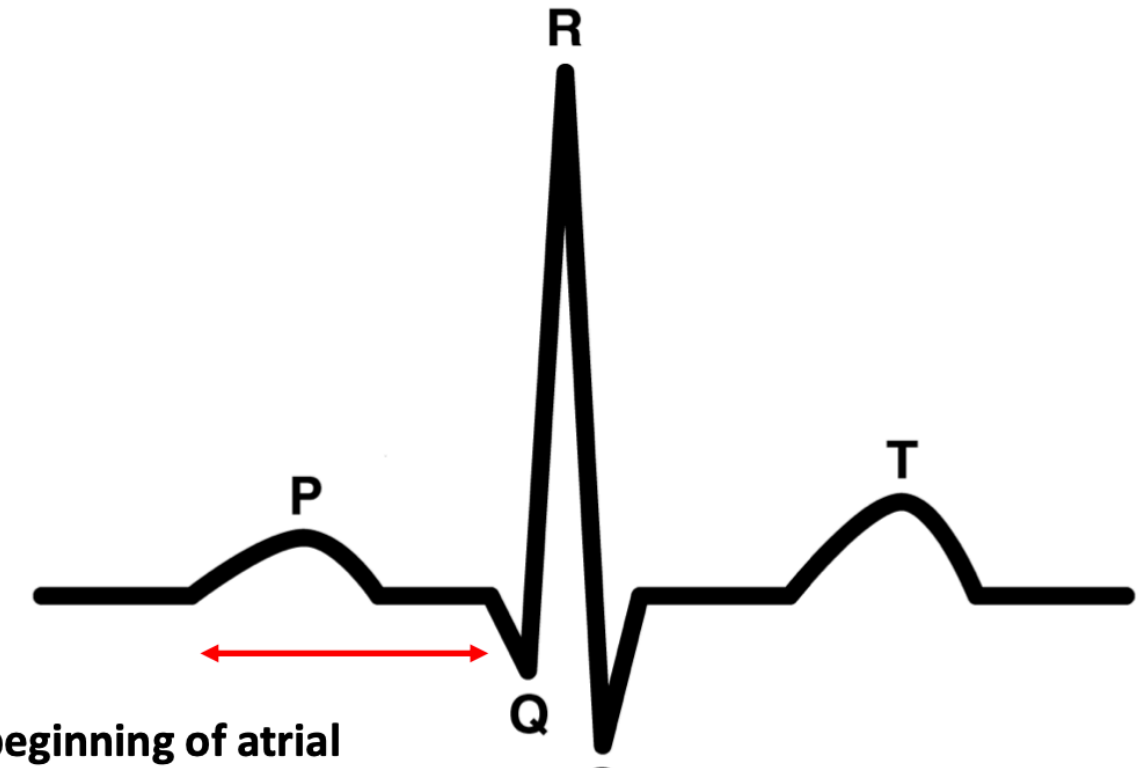
Context

* Complete understanding of rhythm identification is not necessary
* Knowledge of rhythm-related pathophysiology and pharmacology will be very useful

Foundation

* (Sinus Node)
* **Atrial depolarization = P**
* (AV node, His Purkinje, left and right bundles)
* **Ventricular depolarization= QRS**
* (Atrial repolarization)
* **Ventricular repolarization = T**



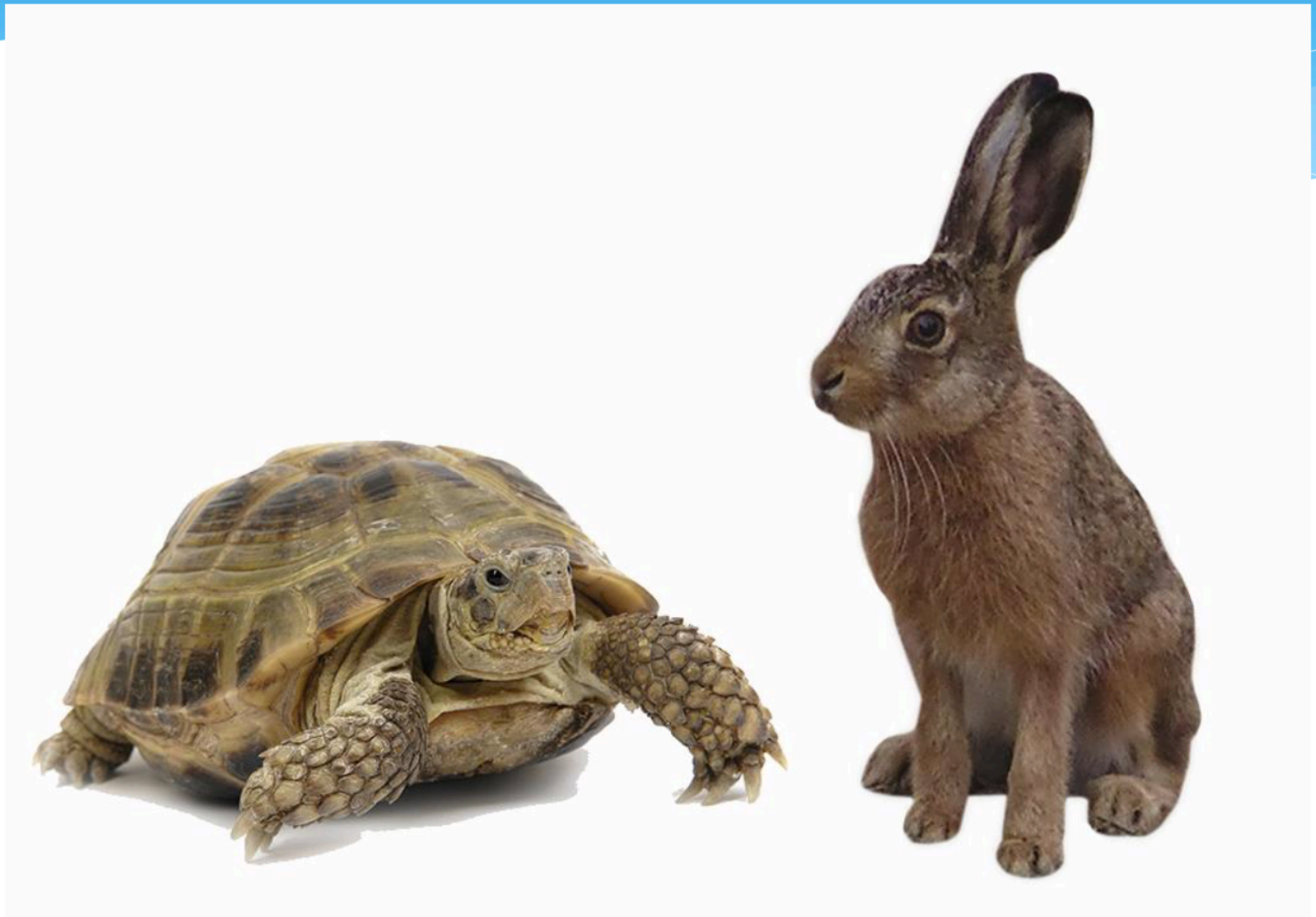


PR interval: beginning of atrial depol to beginning of ventricular depol

QRS duration: ventricular depolarization

QT interval: beginning of ventricular depol to end of ventricular repol

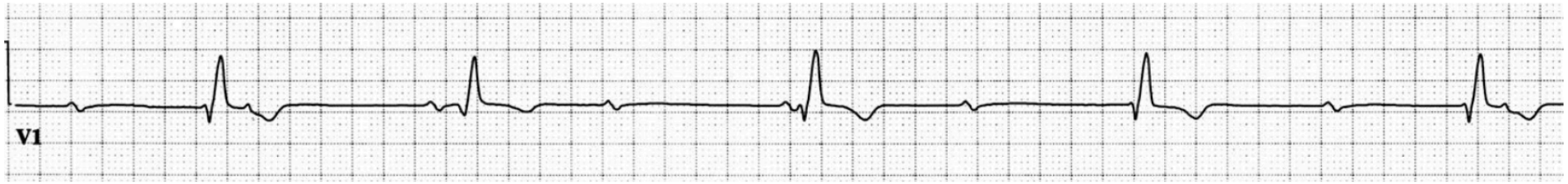
Cardiac Arrhythmias

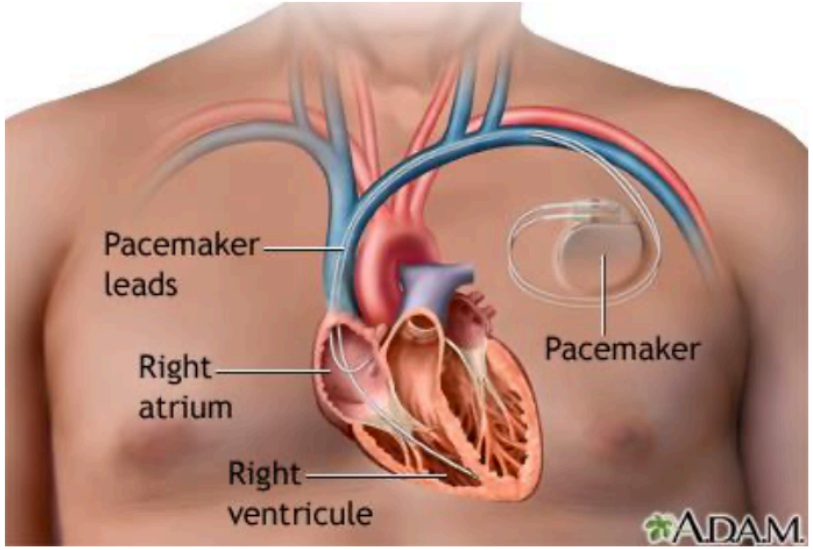


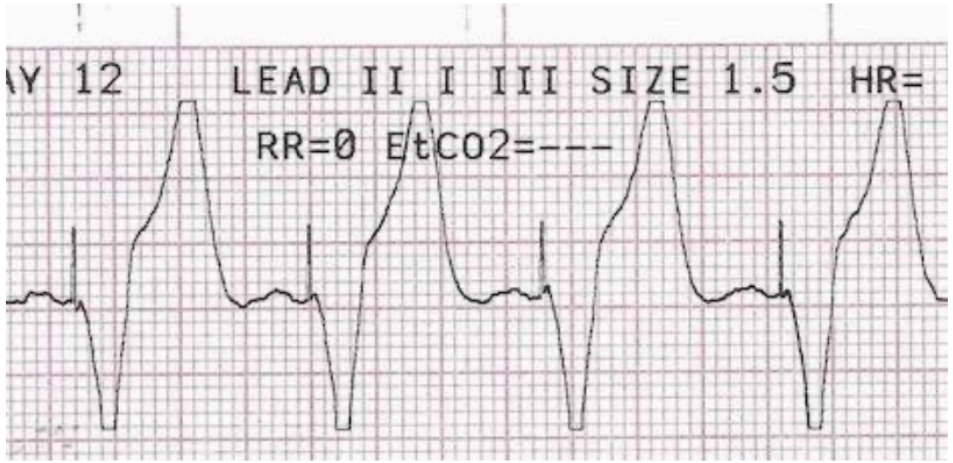
Bradyarrhythmias

* Heart rate is too slow
  * Impulse generation (sinus bradycardia)
  * Impulse conduction (complete AV block)
* Common causes: age-related degeneration, drug effects, hypothyroidism, Lyme disease
* Treatment: reverse underlying cause or pacemaker

Complete Heart Block



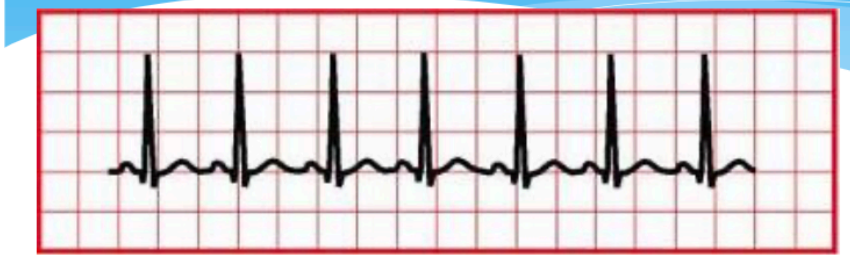




Tachyarrhythmias

* Heart rate is too fast
* Two main mechanisms
  * Automatic arrhythmias
  * Re-entrant arrhythmias

Automatic Tachycardias

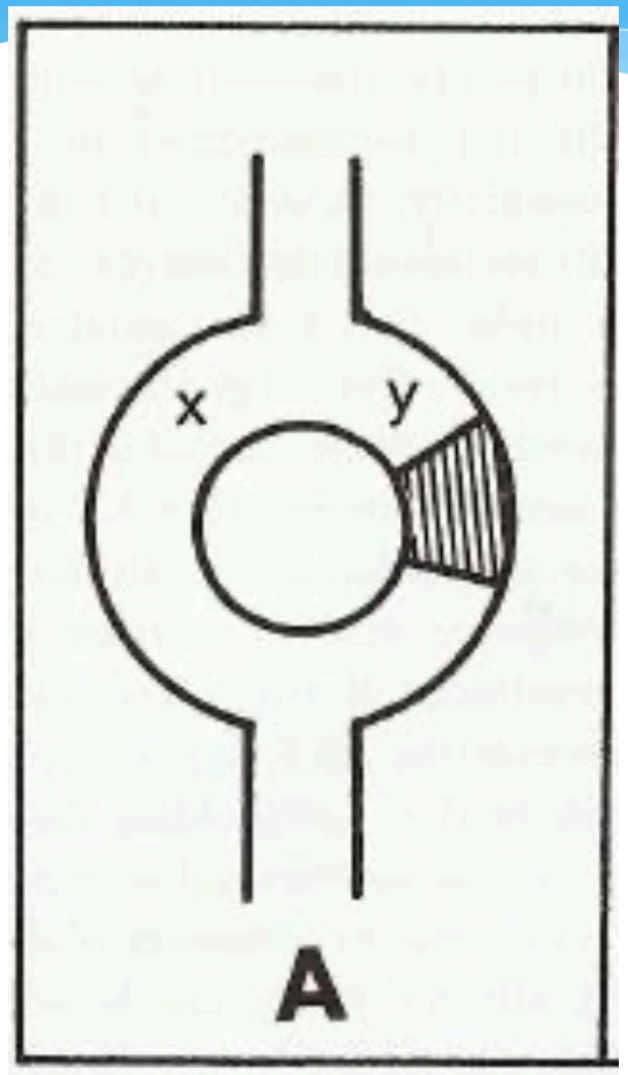


* Focal area within the heart depolarizing at a rapid rate
* Most common example: sinus tachycardia!
* Atrial tachycardia, rare forms of ventricular tachycardia
* Common causes of AT: systemic illness, hyperthyroidism, lung disease, atrial dilation
* Treatment: β or Ca^{++} blockers, ablation

Re-entry

* Complicated but important concept
* Underlies how many arrhythmias are treated, including the use of antiarrhythmic drugs
* Re-entrant arrhythmias also called circus movement tachycardias

Re-entry

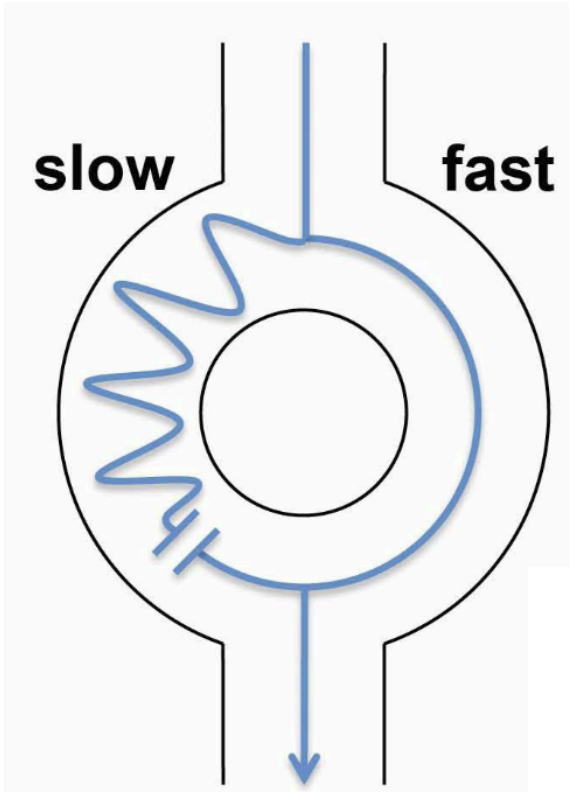


* Common entry point
* Two potential pathways with different:
  * Conduction speeds
  * Refractory periods
* Common exit point

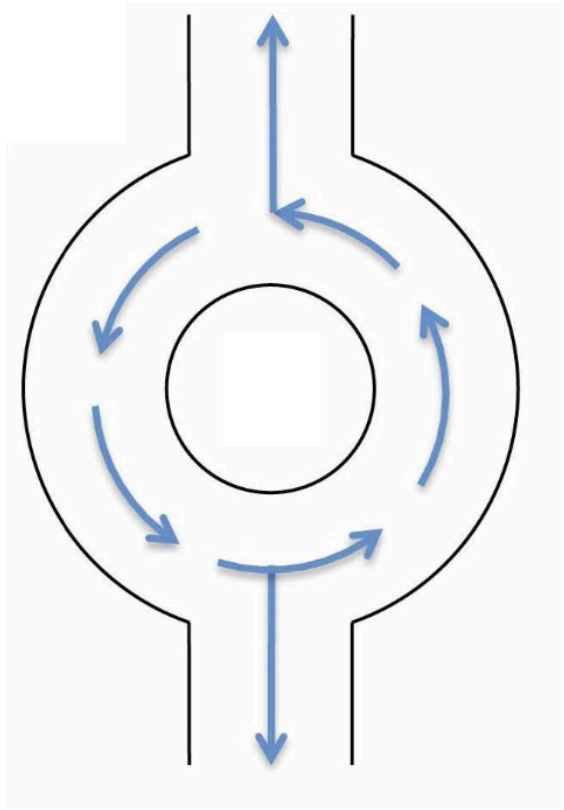
* This loop can exist in many locations within the heart.

Re-entry

Baseline



Tachycardia



Examples of Re-entry Rhythms

* Wolf-Parkinson-White tachycardia
* AV nodal re-entrant tachycardia
* Atrial flutter
* Ventricular tachycardia (most common forms)
* Pacemaker-mediated tachycardia

* Atrial fibrillation (certain aspects)

Treatment of Re-entry Rhythms

* Antiarrhythmic drugs work by changing the electrical properties of the re-entry loop, so that circular electrical activity can no longer be sustained
* Ablation can physical destroy part of the re-entry loop.

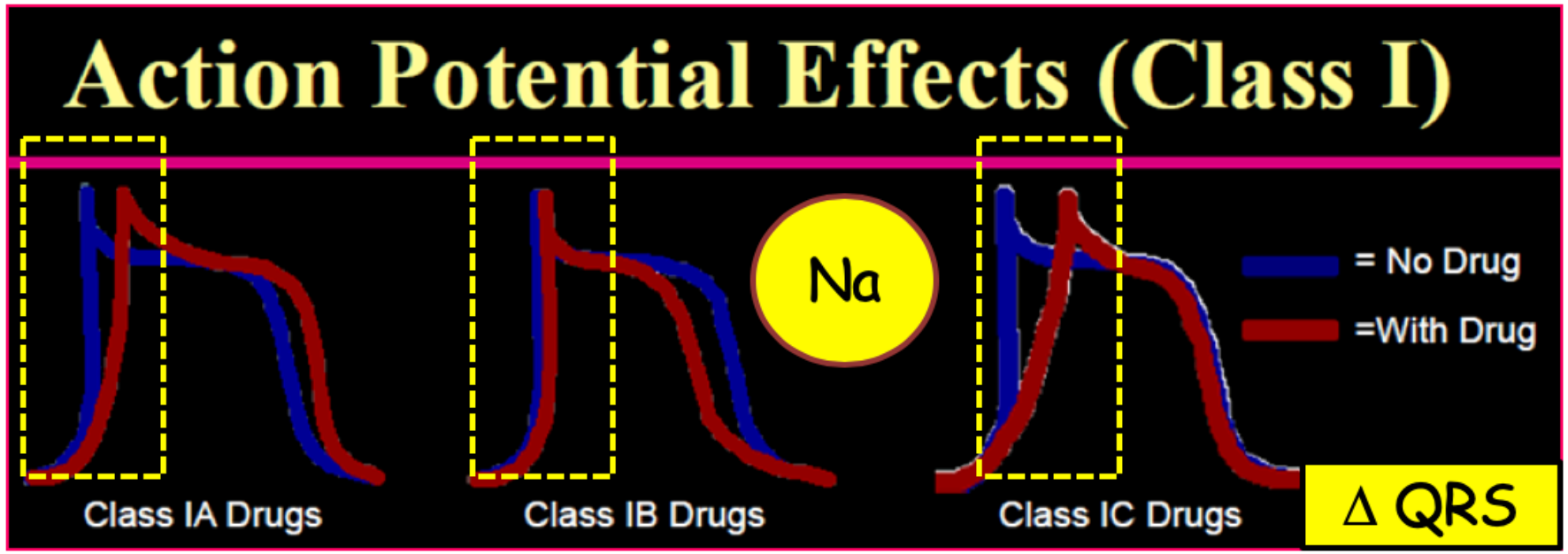
Anti-arrhythmic Drugs

* True AADs alter the myocyte action potential by blocking Na^+ or K^+ channels
* Though drug mechanisms often described 'purely,' many drugs interact with multiple receptors
* AADs can actually cause arrhythmias!
  * Drugs that have K^+ channel activity will prolong repolarization (QT interval) and may lead to TdP
  * "Bystander" re-entry loops, usually in the LV, may become malignant

Vaughan Williams Classifications

* Class I – Na^+ channel blockers
* Class II – β blockers
* Class III – K^+ channel blockers
* Class IV – Ca^{++} blockers
* Class V – misc

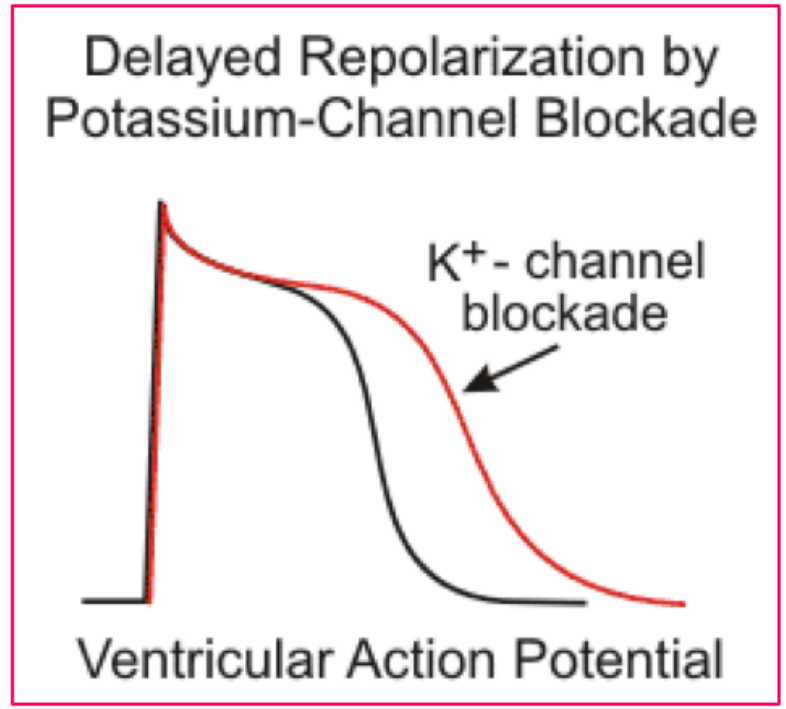
Antiarrhythmic drugs worth knowing – for boards and career!



K^+

Class III

Δ QT interval



Antiarrhythmics: Class I (Na)

P
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c

1a. Procainamide

1b. Lidocaine

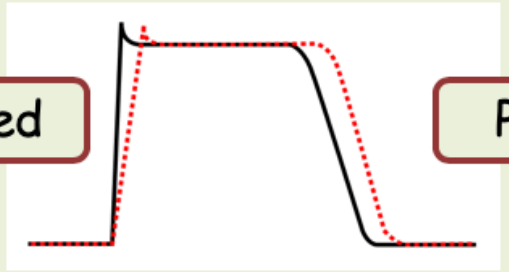
1c. Flecainide

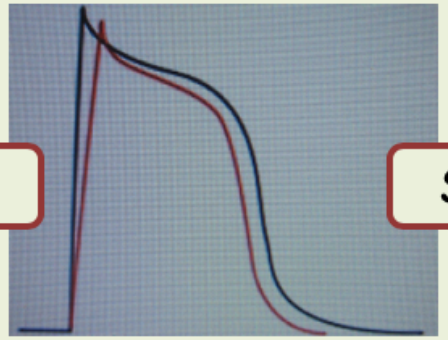
Antiarrhythmics: Class I (Na)

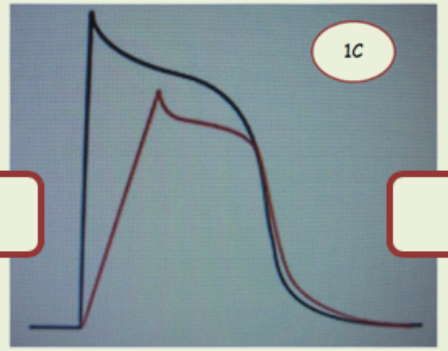
		Phase 0 Inhibition	AP Duration
P r o L i F i c	1a. Procainamide Old	Intermed	Prolongs
	1b. Lidocaine MI	Weak	Shortens
	1c. Flecainide New	Strong	No Δ

Antiarrhythmics: Class I (Na)

		Phase 0 Inhibition	AP Duration
P r o L i F i c	1a. Procainamide Old	Intermed	Prolongs
	1b. Lidocaine MI	Weak	Shortens
	1c. Flecainide New	Strong	No Δ



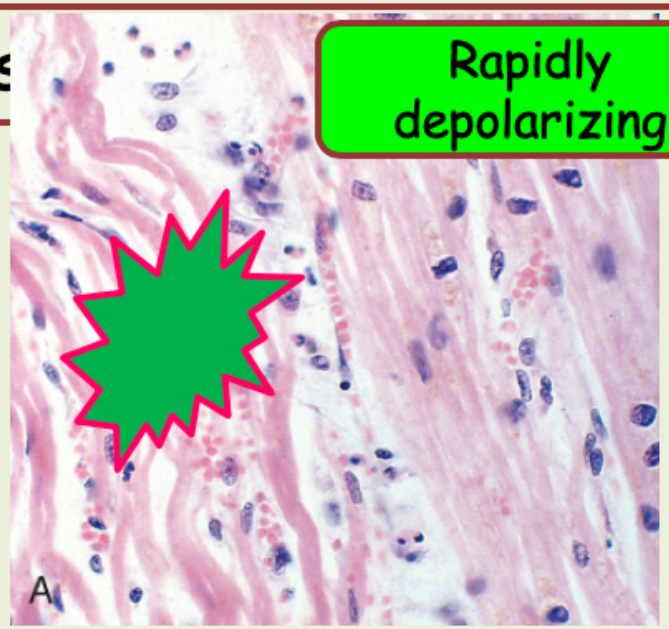


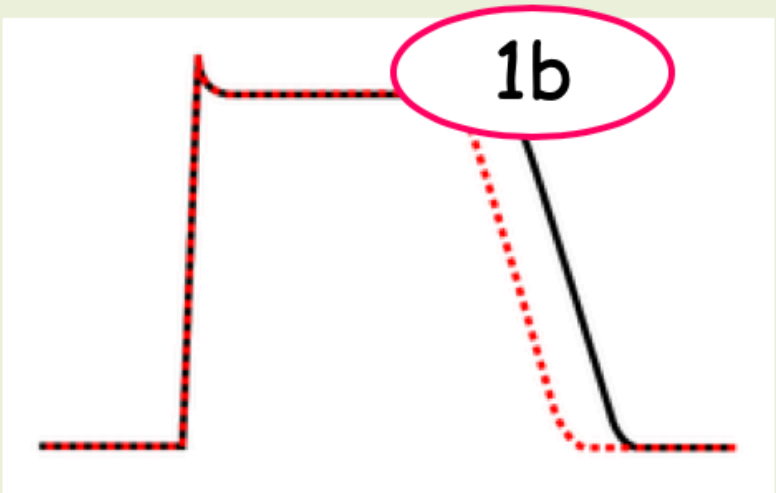


Antiarrhythmics: Class

P r o L i

1b. Lidocaine
Mexilitine





- Slight Phase 0 inhibition
- AP duration – no Δ
- **Fast on/fast off**
- Safe peri-infarction

Antiarrhythmics: Class I (Na)

P
r
o
L
i
F
i
c

1a. Procainamide
Quinidine
Disopyramide

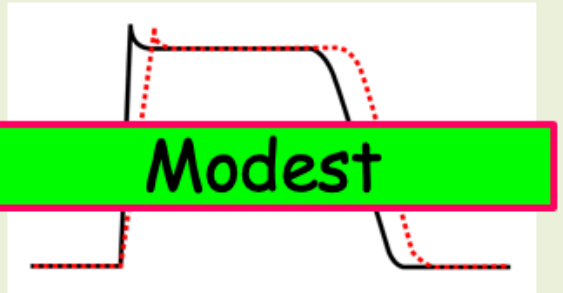
1c. Flecainide
Propafanone

Antiarrhythmics: Class I (Na)

P r o L i F i c

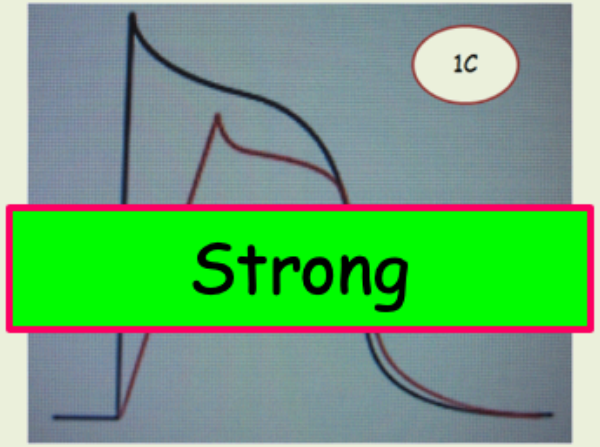
Na Channel Effect
(Phase 0 depolarization)

1a. Procainamide
Quinidine
Disopyramide



Modest

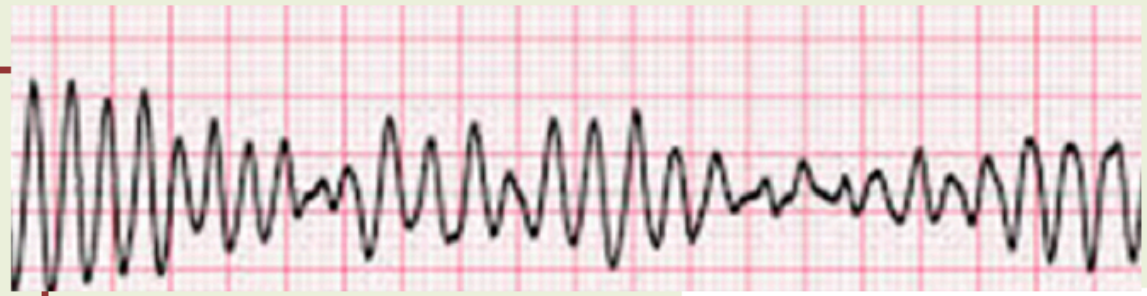
1c. Flecainide
Propafanone



Strong

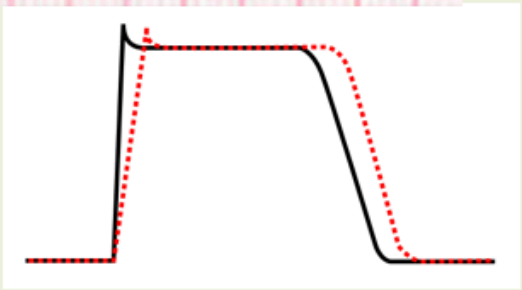
Antiarrhythmics: Class I (Na)

Pro Li Fi c



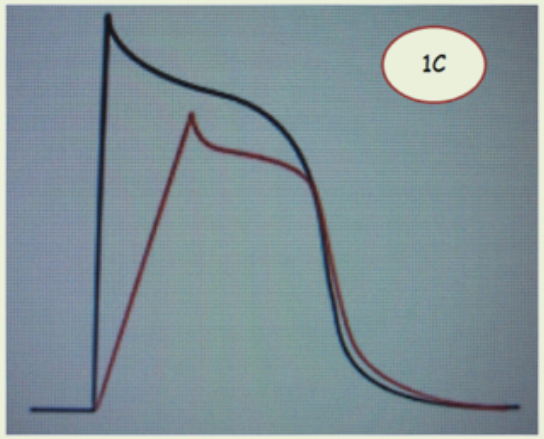
AP duration

1a. Procainamide
Quinidine
Disopyramide



Prolonged

1c. Flecainide
Propafanone



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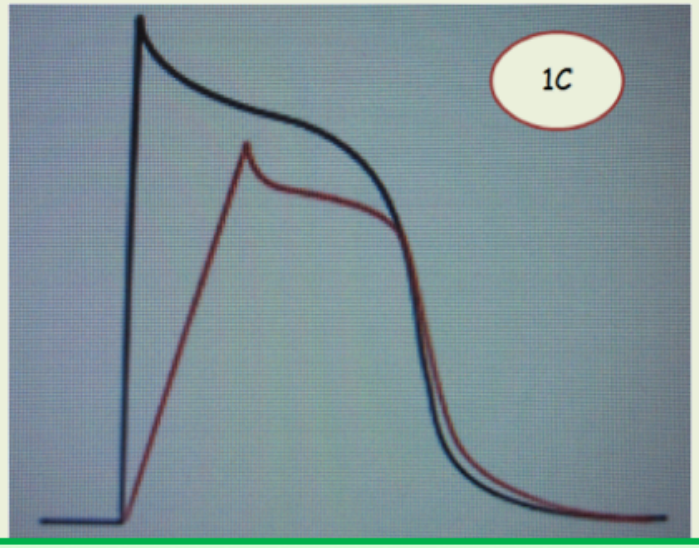
Antiarrhythmics: Class I (Na)

P r o L

1c. Flecainide
Propafanone



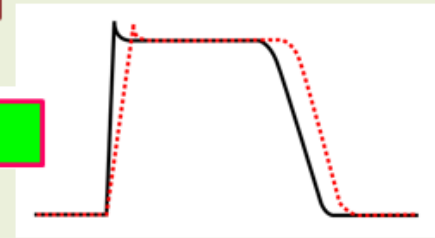
'Use Dependence'

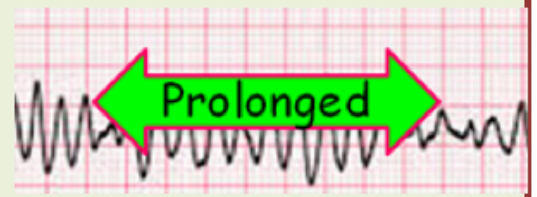
- Slowly dissociates from Na channel during diastole.
- At faster HR (less diastole), less time to dissociate, with enhanced Na channel blocking effects.
- QRS widens, but AP duration remains the same

P r o L i F i c

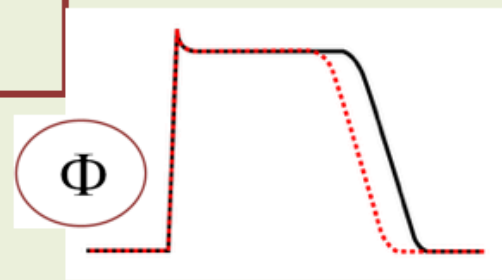
1a. Procainamide

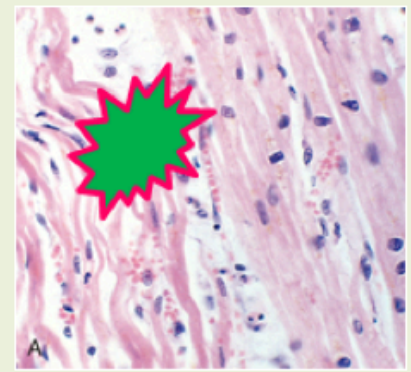
Modest



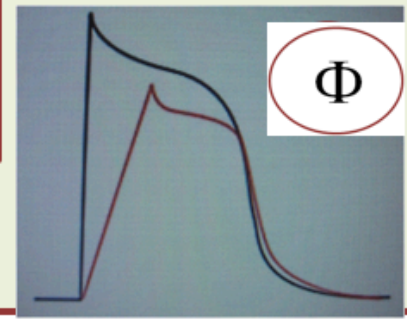


1b. Lidocaine



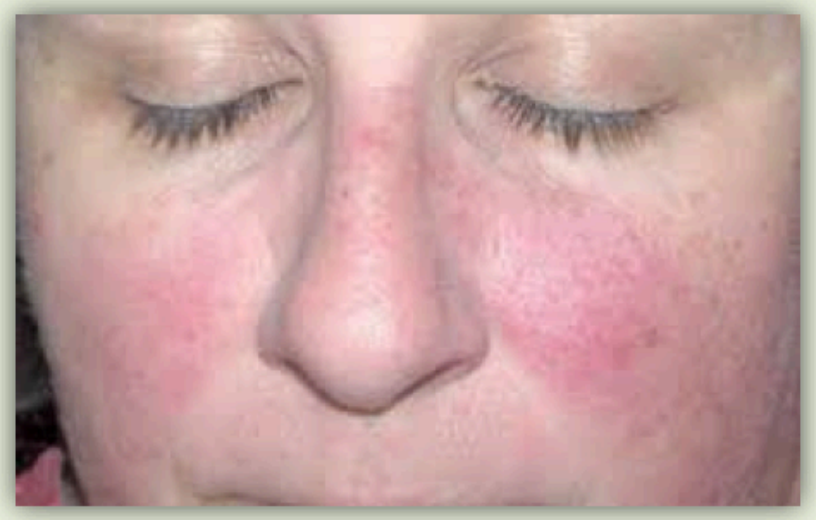


1c. Flecainide



PrOLiFic

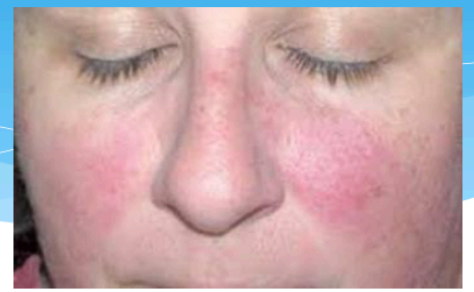
1a. Procainamide



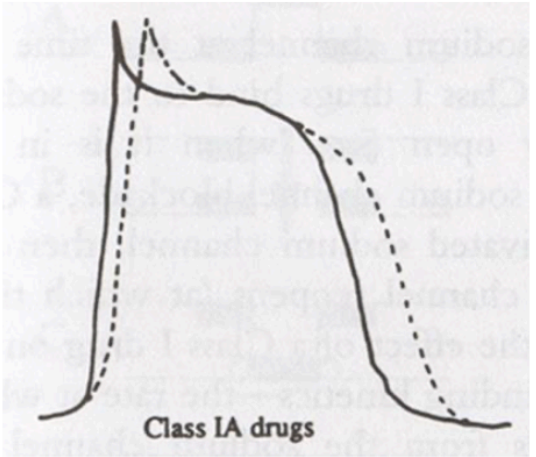
Anti-histone Aby

Slow acetylators

Procainamide

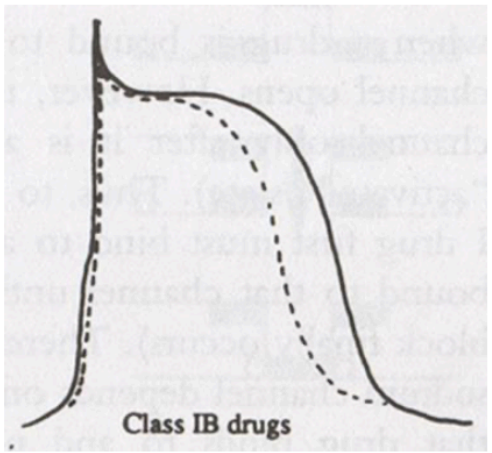


* Class 1A agent
* Metabolized to NAPA, with longer half life
* Modestly effective, modestly pro-arrhythmic
* Associated with drug-induced lupus and anti-histone ab production
* Limited contemporary clinical use



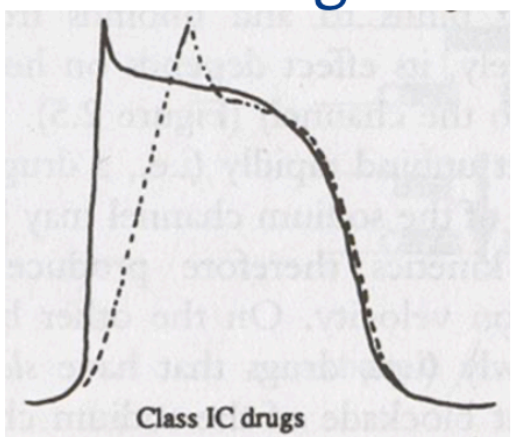
Lidocaine & Mexilitine

* Class 1B agents
* Safe and effective for ventricular dysrhythmias, including in the context of myocardial ischemia
* Limited contemporary clinical use



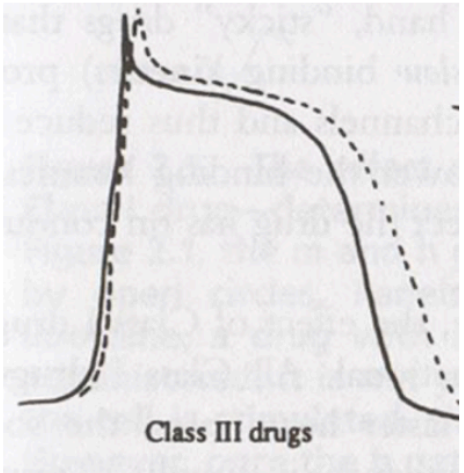
Flecainide & Propafenone

* Class 1 C agents
* Predominantly used for atrial fibrillation
* Demonstrates phenomenon of "use dependence"
  * Dissociation from Na channels is time-dependent
  * Therefore, less dissociation at higher heart rates
  * With tachycardia, may see more pronounced drug effects (i.e., QRS widening)



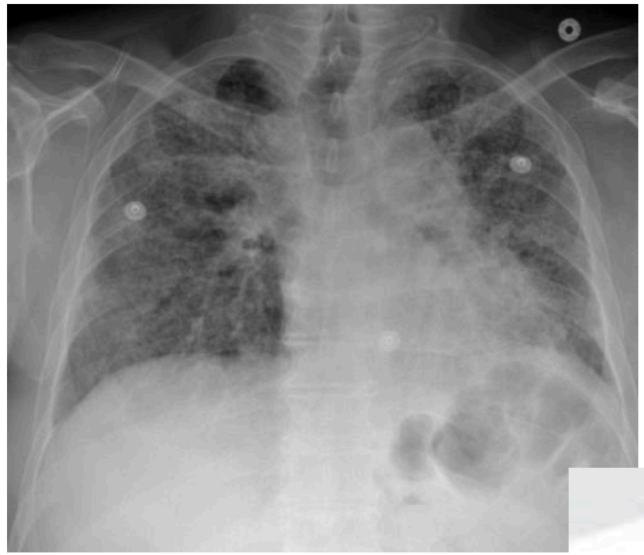
Sotalol & Dofetilide

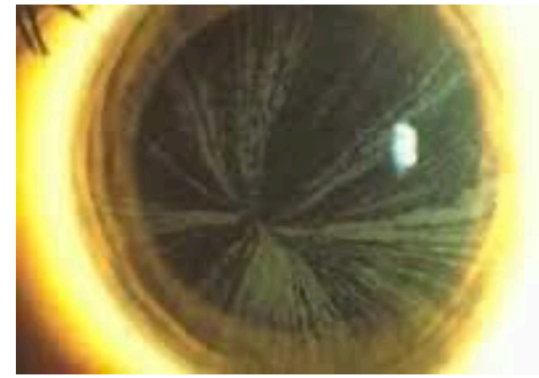
* Class III – sotalol also with significant beta blocking effects
* Effective for atrial (dofetilide) and atrial and ventricular dysrhythmias (sotalol)
* Demonstrates "reverse use dependence"
  * Easier to remember that QT prolongation is expected, and will be more pronounced at slower heart rates
* Renal clearance



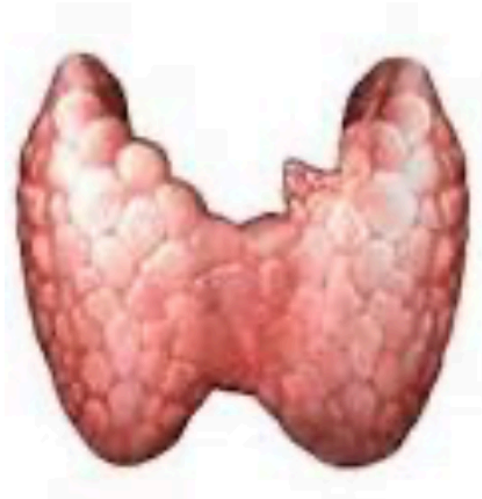
Amiodarone

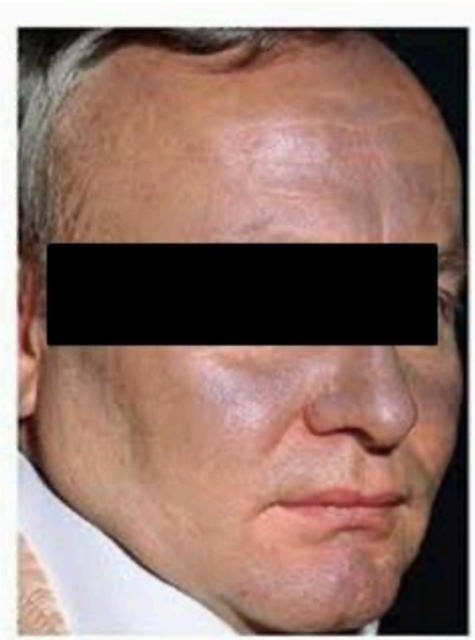
* Class III, but multiple mechanisms of action
* Remarkably effective drug for many dysrhythmias
* Prolongs QT interval, but low incidence of TdP
* Multiple potential toxicities, especially with higher cumulative doses






Amiodarone
200 mg tablets



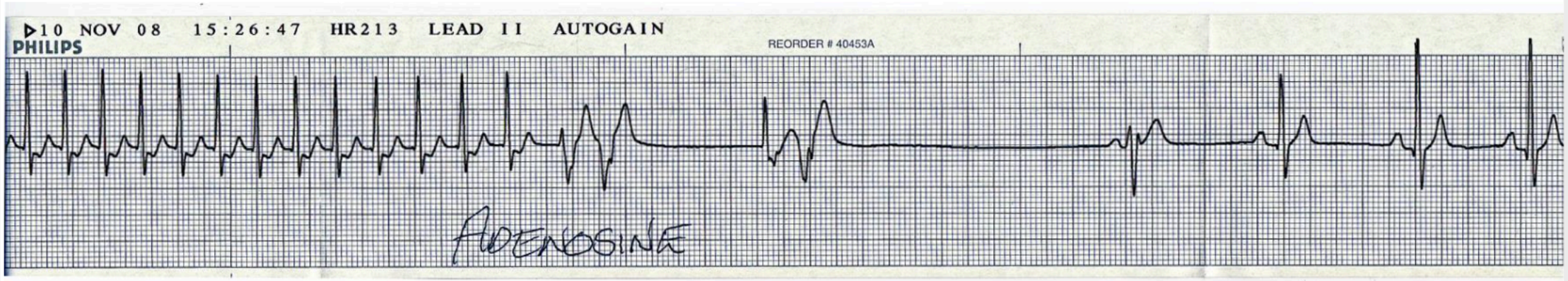


Adenosine

* Miscellaneous agent
* Activates A_1 receptor in heart, causing transient (seconds) complete AV block
* MoA: excessive K^+ efflux in the AVN → cell hyperpolarization (but Na^+ and Ca^+ currents likely also involved)
* Also has vasodilatory properties, especially in coronary circulation
* How might such action be useful clinically?

Adenosine

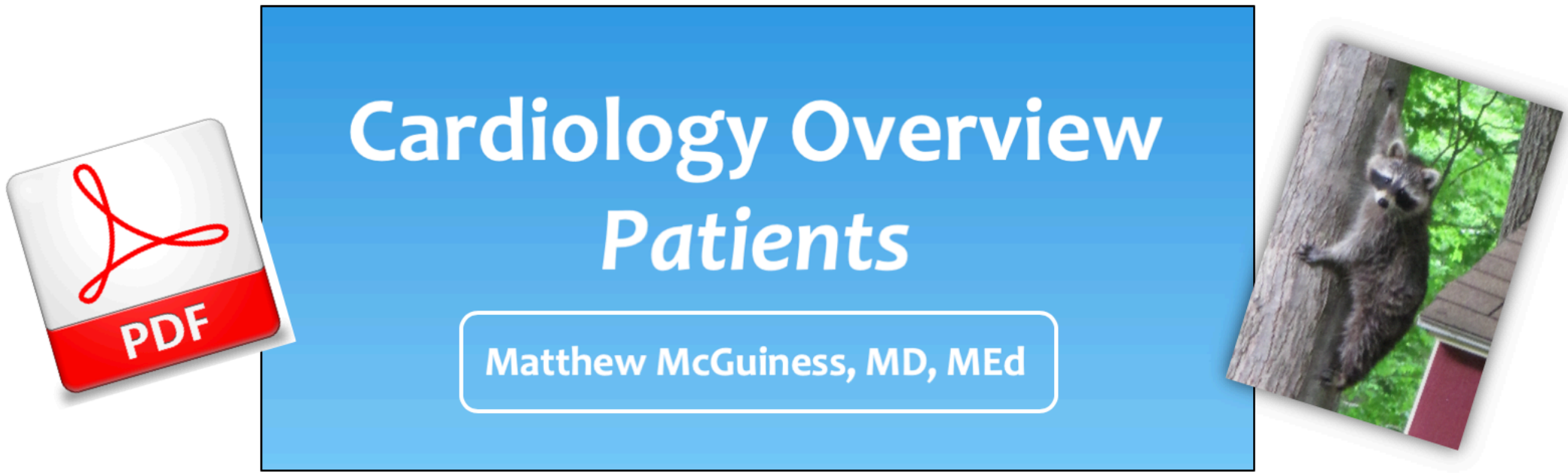
* Therapeutically
* Diagnostically



Summary

* Arrhythmias can be categorized as slow or fast
* Tachycardias may have an automatic or re-entry mechanism
* Principle of re-entry underlies the pathogenesis and treatment of many dysrhythmias
* Antiarrhythmic drugs can be safe and effective, but carry risks, and must be used cautiously

Cardiac Electrophysiology for the USMLE Step One Exam



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